

Ice-binding proteins for cryopreservation of heart cells and tissue

Daniëlle van den Broek MSc, prof.dr.ir. Ilja Voets

Self-Organizing Soft Matter – Eindhoven University of Technology

The high global prevalence of heart failure creates an urgent need for donor hearts. Currently 70% of the available donor hearts cannot be used for transplantation,¹ due to the limited preservation time of 4-6 hours in conventional cold storage.² Long-term storage in a frozen state (cryopreservation) would provide a solution, but the formation of ice crystals in the tissue results in irreparable freezing damage. The use of ice-binding proteins is a promising strategy to protect the organ.^{3,4} Natural ice-binding proteins from cold-adapted organisms modulate the size and shape of ice crystals, but they are not evolved for cryopreservation. In our research we will characterize the activity of both natural ice-binding proteins⁵ and modified versions, to elucidate how the protein structure induces the different forms of ice-binding activity: ice recrystallization inhibition,⁶ crystal shaping, thermal hysteresis⁴ and ice nucleation.⁷ Ultimately, we will apply this knowledge to engineer novel ice-binding proteins that are optimized to protect heart cells and tissue against freezing damage.

Acknowledgements:

Roderick Tas, Tim Hogervorst, Marco Hendrix, Ilja Voets (Self-Organizing Soft Matter – Eindhoven University)

Carlijn Bouten, Atze van der Pol (Soft Tissue Engineering and Mechanobiology – Eindhoven University)

Vasco Sampaio Pinto, Linda van Laake (Cardiology – Utrecht University Medical Center)
European Research Council

References:

1. Giwa, S. *et al.* The promise of organ and tissue preservation to transform medicine. *Nature Biotechnology* **35** 530–542 (2017).
2. Guibert, E. E. *et al.* Organ preservation: Current concepts and new strategies for the next decade. *Transfusion Medicine and Hemotherapy* **38**, 125–142 (2011).
3. Sampaio-Pinto, V. *et al.* A Roadmap to Cardiac Tissue-Engineered Construct Preservation: Insights from Cells, Tissues, and Organs. *Advanced Materials* **33**, (2021).
4. Tas, R. P., Sampaio-Pinto, V., Wennekes, T., Laake, L. W. & Voets, I. K. From the freezer to the clinic. *EMBO Rep* **22**, (2021).
5. Bar Dolev, M., Braslavsky, I. & Davies, P. L. Ice-Binding Proteins and Their Function. in *Annual Review of Biochemistry* **85**, 515–542 (2016).
6. Budke, C. *et al.* Quantitative efficacy classification of ice recrystallization inhibition agents. *Crystal Growth and Design* **14**, 4285–4294 (2014).
7. Eickhoff, L. *et al.* Contrasting Behavior of Antifreeze Proteins: Ice Growth Inhibitors and Ice Nucleation Promoters. *Journal of Physical Chemistry Letters* **10**, 966–972 (2019).